

IN THE CLAIMS

Please amend the claims as follows:

1. (Original) In a coagulation assay comprising combining a coagulation assay reagent and a whole blood sample or plasma sample and obtaining a coagulation assay measurement, by adding to a dry coagulation assay reagent containing magnetic particles distributed substantially homogeneously therethrough, arranged in a substantially flattened format, and under the influence of an oscillating magnetic field or moving permanent magnetic field, or both, a whole blood sample or a plasma sample thereby substantially simultaneously initiating movement of said magnetic particles and the coagulation assay measurement and monitoring movement of said magnetic particles to obtain said assay measurement, wherein the improvement comprises adding to said dry coagulation assay reagent one or more metal compounds that interact with calcium binding sites in a blood coagulation cascade.

2. (Original) In the coagulation assay of claim 1, wherein the one or more metal compounds are a member selected from the group consisting of compounds of magnesium, manganese, europium, lanthanum, gadolinium and terbium.

3. (Original) A method for performing a coagulation assay on a whole blood or plasma sample, comprising:

(i) adding a first, whole blood or plasma, component of the assay to a second component of the assay, wherein said second component comprises a dry coagulation assay reagent arranged in a substantially flattened configuration and containing magnetic particles distributed substantially homogeneously therethrough, and wherein said second is subjected to (ia) an

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

oscillating magnetic field or (ib) a moving permanent magnetic field or (ic) a combination of an oscillating magnetic field and a stationary permanent magnetic field or (id) a rotating magnetic field, whereby said adding of said first component to said second component substantially simultaneously initiates movement of said magnetic particles and the coagulation assay measurement; and

(ii) monitoring movement induced in said magnetic particles by (ia) or (ib) or (ic) or (id) to obtain said coagulation assay measurement,

wherein said dry coagulation assay reagent comprises a coagulation initiator and one or more metal compounds that interact with calcium binding sites in a blood coagulation cascade.

4. (Original) The method of claim 3, wherein said coagulation assay is a clotting assay.

5. (Original) The method of claim 4, wherein said sample is whole blood.

6. (Original) The method of claim 4, wherein said sample is plasma.

7. (Original) The method of claim 4, wherein said magnetic particles are induced to move by applying an oscillating magnetic field thereto.

8. (Original) The method of claim 4, wherein said magnetic particles are induced to move by applying a moving permanent magnetic field thereto.

9. (Original) The method of claim 4, wherein said coagulation initiator comprises thromboplastin and a calcium salt.

10. (Original) The method of claim 3, wherein said method is carried out in an element for performing said coagulation assay, said method comprising adding said sample to said element, wherein said element comprises a channel structure defining a sample well and

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

a reaction volume in fluid communication with each other, said reaction volume containing said second component, said channel structure having a geometry causing said sample placed in said sample well to be drawn into and filling said reaction volume via capillary action, wherein, after said reaction volume is filled, said sample remains stationary therein.

11. (Original) The method of claim 10, wherein said element further comprises a means for channeling light from an outside source to said reaction volume.

12. (Original) The method of claim 11, further comprising using a means for detecting light scattered or absorbed or reflected from said reaction volume.

13. (Original) The method of claim 10, wherein said element is disposed in sufficiently close proximity to a permanent magnet and to an electromagnet such that said permanent magnet and said electromagnet provide said combination of an oscillating magnetic field and a stationary permanent magnetic field.

14. (Original) The method of claim 13, wherein said element is situated between said permanent magnet and said electromagnet.

15. (Original) The method of claim 10, wherein said magnetic particles are induced to move by application of a rotating magnetic field.

16. (Original) The method of claim 3, wherein said metal compound is a lanthanide compound.

17. (Original) The method of claim 3, wherein said metal compound is a member selected from the group consisting of compounds of magnesium, manganese, europium, lanthanum, gadolinium and terbium.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

18. (Original) A method for performing a coagulation assay measurement, comprising:
- (i) adding a whole blood or plasma sample to the sample well of an element comprising: a channel structure defining a sample well and a reaction volume in fluid communication with each other, wherein said reaction volume is defined by an upper surface having attached thereto a reflectance layer, comprising a semipermeable matrix wherein said reaction volume contains a measured amount of at least one dry coagulation assay reagent arranged in a substantially flattened configuration and containing magnetic particles distributed substantially homogeneously therethrough, wherein a specific volume of said sample is drawn into said reaction volume by capillary action and contacts, together with said semipermeable layer, said reagent to thereby substantially simultaneously initiate said coagulation assay measurement; and
- (ii) performing said coagulation assay measurement by measurement the reflectance of said semipermeable layer,
wherein said dry coagulation assay reagent comprises a coagulation initiator and one or more metal compounds that interact with calcium binding sites in a blood coagulation cascade.

19. (Original) The method of claim 18, wherein said one or more metal compounds is a lanthanide compound.

20. (Original) The method of claim 18, wherein said one or more metal compounds is a member selected from the group consisting of compounds of magnesium, manganese, europium, lanthanum, gadolinium and terbium.

21. (Currently Amended) A dry coagulation assay reagent comprising magnetic

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

particles distributed substantially homogeneously therethrough wherein said reagent is selected from the group consisting of:

- (1) one member selected from the group consisting of prothrombin time reagents and (ii) prothrombin time reagents and calcium salts;
- (2) partial thromboplastin time reagents with calcium chloride;
- (3) partial thromboplastin time reagents with calcium chloride and clot formation activators;
- (4) thrombin or a snake venom with thrombotic activity;
- (5) fibrin, or plasminogen and fibrin;
- (6) plasminogen activator assay reagents containing (i) plasminogen and (ii) either fibrin, a snake venom with thrombotic activity, or thrombin;
- (7) plasminogen assay reagents containing (i) a plasminogen activator and (ii) either fibrin, a snake venom with thrombotic activity, or thrombin;
- (8) natural and synthetic plasminogen activators;
- (9) alpha -2-antiplasmin assay reagents containing fibrin and plasmin; and
- (10) combinations thereof,

wherein the reagent further comprises one or more lanthanide metal compounds that interact with calcium binding sites in a blood coagulation cascade.

Claim 22. (Cancel)

23. (Currently Amended) The reagent of claim 21, wherein said one or more lanthanide metal compounds are selected from the group consisting of compounds of ~~magnesium, manganese~~, europium, lanthanum, gadolinium and terbium.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

24. (Currently Amended) The reagent of claim 21, wherein said one or more lanthanide metal compounds are selected from the groups group consisting of salts of organic acids, halides, C2-C6 alkyl esters of organic acids, hexafluorophosphates, nitrates, oxalates, perchlorates, tetrafluoroborates, trifluoromethanesulfonates, substituted and unsubstituted C4-C8 alkanedionates, acetylacetones, and sulfates.

25. (Original) The reagent of claim 21, wherein said reagent is thromboplastin or thromboplastin and a calcium salt.

26. (Original) The reagent of claim 21, wherein said reagent is a partial thromboplastin time reagent with calcium chloride.

27. (Original) The reagent of claim 21, wherein said reagent is a partial thromboplastin reagent with calcium chloride and a clot formation activator.

28. (Original) The reagent of claim 21, wherein said reagent is thrombin or a snake venom with thrombotic activity.

29. (Original) The reagent of claim 21, wherein said reagent is fibrin, plasminogen and fibrin, a snake venom with thrombin-like activity, or thrombin.

30. (Original) The reagent of claim 29, comprising either said snake venom with thrombotic activity or a combination of said snake venom with thrombotic activity and thrombin.

31. (Original) The reagent of claim 21, wherein said reagent is a plasminogen assay reagent containing (i) a plasminogen activator and (ii) either fibrin, a snake venom with thrombotic activity, or thrombin.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

32. (Original) The reagent of claim 31, comprising either said snake venom with thrombotic activity or a combination of said snake venom with thrombotic activity and thrombin.

33. (Original) The reagent of claim 21, wherein said reagent is one member selected from the group consisting of streptokinase and urokinase.

34. (Original) The reagent of claim 21, wherein said reagent comprises one member selected from the group consisting of natural and synthetic tissue plasminogen activators.

35. (Original) The reagent of claim 21, wherein said reagent is an alpha -2-antiplasmin assay reagent containing fibrin and plasmin.

36. (Original) The reagent of claim 21, wherein said reagent comprises:
(4) thrombin or a snake venom with thrombotic activity; and
(8) one member selected from the group consisting of natural and synthetic plasminogen activators.

37. (Original) The reagent of claim 21, wherein said reagent comprises at least one member selected from the group consisting of streptokinase, tissue plasminogen activator and urokinase.

38. (Original) A kit for performing a coagulation assay, comprising, in one or more containers, a permanent magnet, a timing means, and an element containing at least one dry coagulation assay reagent arranged in a substantially flattened format and containing magnetic particles distributed substantially homogeneously therethrough, wherein said at least one dry coagulation assay reagent comprises a coagulation initiator and one or more metal compounds that interacts with calcium binding sites in a blood coagulation cascade.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

39. (Original) The kit of claim 38, wherein said one or more metal compounds is a lanthanide compound.

40. (Original) The kit of claim 38, wherein said one or more metal compounds are selected from the group consisting of compounds of magnesium, manganese, europium, lanthanum, gadolinium and terbium.

41. (Original) The kit of claim 38, further comprising a transfer pipette.

42. (Original) A system for performing a coagulation assay measurement, comprising:

- (i) an instrument with a means for temperature control, a means for producing an oscillating magnetic field or for moving a permanent magnetic field, an illuminating means, and a photometric monitoring means; and
- (ii) an element for performing said coagulation assay, said element comprising a channel structure defining a sample well and reaction volume in fluid communication with each other, said channel structure having a geometry causing a liquid sample placed in said sample well to be drawn into and filling said reaction volume via capillary action, said reaction volume comprising at least one dry coagulation assay reagent arranged in a substantially flattened configuration and containing magnetic particles distributed substantially homogeneously therethrough, wherein said at least one dry coagulation assay reagent comprises a coagulation initiator and one or more metal compounds that interact with calcium binding sites in a blood coagulation cascade.

43. (Original) The system of claim 42, wherein said one or more metal compounds is a lanthanide compound.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

44. (Original) The system of claim 42, wherein said one or more metal compounds are selected from the group consisting of compounds of magnesium, manganese, europium, lanthanum, gadolinium and terbium.

45. (Original) The system of claim 42, further comprising a transfer pipette.

46. (Original) The system of claim 42, wherein said transfer pipette is made of an essentially nonthrombogenic material, comprises a vented end, is capable of being filled with a liquid sample by capillary action, and is capable of expelling said liquid sample by means of pressure after covering or sealing said vented end.

47. (Original) The system of claim 42, wherein said instrument further comprises a heating means comprising a resistive heater strip and a thermistor situated in close proximity to said element.

48. (Original) The system of claim 42, wherein said element is suitable for performing a whole blood coagulation assay, said channel structure having a geometry causing a blood sample placed in said sample well to be drawn into and filling said reaction volume via capillary action, wherein after said reaction volume is filled, said blood sample remains stationary therein, and wherein said element further comprises an optically or magnetically encodable information means, or both, capable of providing at least one of calibration, quality control, test parameter and patient information.

49. (Original) The system of claim 42, wherein said illuminating means includes one or more light sources to illuminate said element and wherein said photometric monitoring means comprises one or more detectors for photometrically monitoring chromogenic or chromomodulating species present in said reaction volume.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

50. (Original) A system for performing a coagulation assay, comprising:

- (i) a reaction element comprising (1) a sample well for receiving a liquid sample and (2) a reaction chamber containing a dry coagulation assay reagent arranged in a substantially flattened configuration and in which is embedded, substantially homogeneously therethrough, magnetic particles;
- (ii) said sample well and said reaction chamber being in fluid communication through a transport zone of geometry such that a volume of liquid sample placed in said sample well and corresponding to the volume of said reaction chamber is transported from said sample well to said reaction chamber simultaneously;
- (iii) means for optically monitoring said reaction chamber;
- (iv) means for subjecting said reaction chamber to an oscillating magnetic field;
- (v) whereby, when said sample is introduced into said reaction chamber, said dry coagulation assay reagent is solubilized and said magnetic particles are thereby freed to move in an oscillating pattern induced by said oscillating magnetic field, thus providing a measurement of the kinetics of said coagulation assay corresponding to changes in the degree of said magnetic particles movement relative to said oscillating magnetic field, wherein said dry coagulation assay reagent comprises a coagulation initiator and one or more metal compounds that interact with calcium binding sites in a blood coagulation cascade.

51. (Original) The system of claim 50, wherein said one or more metal compounds is a lanthanide compound.

52. (Original) The system of claim 50, wherein said one or more metal compounds are selected from the group consisting of compounds of magnesium, manganese, europium,

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

lanthanum, gadolinium and terbium.

53. (Original) The system of claim 50, further comprising a means for controlling the moment transport of said liquid sample from said sample well to said reaction chamber is initiated.

54. (Original) The system of claim 50, further comprising a plurality of reaction chambers in fluid communication with said sample well, and means for transporting a whole blood or plasma sample from one of said plurality of reaction chambers to another of said plurality of reaction chambers.

55. (Original) The system of claim 52, wherein said one or more metal compounds is a member selected from the group consisting of europium, lanthanum, gadolinium and terbium.

56. (Original) A method for performing a coagulation assay, comprising:
i) subjecting to an oscillating magnetic field a reaction element bearing (1) a sample well for receiving a whole blood or plasma sample and (2) a reaction chamber containing a dry coagulation assay reagent arranged in a substantially flattened format and in which is embedded, substantially homogeneously therethrough, magnetic particles, said sample well and reaction chamber being in fluid communication through a transport zone of geometry such that a volume of sample placed in said sample well and corresponding to the volume of said reaction chamber is transported from said sample well to said reaction chamber simultaneously;

(ii) adding a whole blood or plasma sample susceptible to coagulation to said sample well whereby at least a part of said sample is introduced simultaneously to said reaction chamber,

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

said reagent is solubilized and said particles are freed to move in an oscillating pattern

induced by said oscillating magnetic field; and

(iii) optically monitoring said reaction chamber to measure kinetics for the coagulation assay corresponding to changes in the degree of said particle movement relative to said magnetic field,

wherein said dry coagulation assay reagent comprises a coagulation initiator and one or more metal compounds that interact with calcium binding sites in a blood coagulation cascade.

57. (Currently Amended) A reagent for performing a Protein C assay, comprising:
an initiator of an intrinsic blood coagulation pathway or Factor X;
a Protein C activator;
calcium ions; and
one or more lanthanide metal compounds that interact with calcium binding sites in a blood coagulation cascade.

58. (Original) The reagent of claim 57, wherein said Protein C activator is a thrombomodulin.

Claim 59. (Cancel)

60. (Currently Amended) The reagent of claim 59, wherein said one or more metal compounds are one or more members selected from the group consisting of compounds of ~~magnesium, manganese, terbium, gadolinium, europium and lanthanum~~.

61. (Original) The reagent of claim 57, further comprising one or more bulkers, stabilizers or both.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

62. (Original) A method for performing a Protein C assay on a citrated whole blood or citrated plasma sample, comprising:

(i) adding a first, citrated whole blood or citrated plasma, component of the assay to a second component of the assay, wherein said second component comprises a dry Protein C assay reagent arranged in a substantially flattened configuration and containing magnetic particles distributed substantially homogeneously therethrough, and wherein said second is subjected to (ia) an oscillating magnetic field or (ib) a moving permanent magnetic field or (ic) a combination of an oscillating magnetic field and a stationary permanent magnetic field or (id) a rotating magnetic field, whereby said adding of said first component to said second component substantially simultaneously initiates movement of said magnetic particles and the Protein C assay measurement; and

(ii) monitoring movement induced in said magnetic particles by (ia) or (ib) or (ic) or (id) to obtain said Protein C assay measurement,

wherein said dry Protein C assay reagent comprises an initiator of an intrinsic blood coagulation pathway or Factor X, a Protein C activator, calcium ions and one or more metal compounds that interact with calcium binding sites in a blood coagulation cascade.

63. (Original) The method of claim 62, wherein said sample is citrated whole blood.

64. (Original) The method of claim 63, wherein said sample is citrated plasma.

65. (Original) The method of claim 62, wherein said magnetic particles are induced to move by applying an oscillating magnetic field thereto.

66. (Original) The method of claim 62, wherein said magnetic particles are induced to move by applying a moving permanent magnetic field thereto.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

67. (Original) The method of claim 62, wherein said Protein C initiator comprises a thrombomodulin.

68. (Original) The method of claim 67, wherein said thrombomodulin is a natural thrombomodulin.

69. (Original) The method of claim 67, wherein said thrombomodulin is a recombinant thrombomodulin.

70. (Original) The method of claim 62, wherein said method is carried out in an element for performing said Protein C assay, said method comprising adding said sample to said element, wherein said element comprises a channel structure defining a sample well and a reaction volume in fluid communication with each other, said reaction volume containing said second component, said channel structure having a geometry causing said sample placed in said sample well to be drawn into and filling said reaction volume via capillary action, wherein, after said reaction volume is filled, said sample remains stationary therein.

71. (Original) The method of claim 70, wherein said element further comprises a means for channeling light from an outside source to said reaction volume.

72. (Original) The method of claim 71, further comprising using a means for detecting light scattered or absorbed or reflected from said reaction volume.

73. (Original) The method of claim 70, wherein said element is disposed in sufficiently close proximity to a permanent magnet and to an electromagnet such that said permanent magnet and said electromagnet provide said combination of an oscillating magnetic field and a stationary permanent magnetic field.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

74. (Original) The method of claim 73, wherein said element is situated between said permanent magnet and said electromagnet.

75. (Original) The method of claim 70, wherein said magnetic particles are induced to move by application of a rotating magnetic field.

76. (Original) The method of claim 62, wherein said metal compound is a lanthanide compound.

77. (Original) The method of claim 62, wherein said metal compound is a member selected from the group consisting of compounds of magnesium, manganese, europium, lanthanum, gadolinium and terbium.

78. (Original) A kit for performing a Protein C assay, comprising, in one or more containers, a permanent magnet, a timing means, and an element containing at least one dry Protein C assay reagent arranged in a substantially flattened format and containing magnetic particles distributed substantially homogeneously therethrough, wherein said at least one dry Protein C assay reagent comprises an initiator of an intrinsic blood coagulation pathway or Factor X, a Protein C activator, calcium ions and one or more metal compounds that interacts with calcium binding sites in a blood coagulation cascade.

79. (Original) The kit of claim 78, wherein said one or more metal compounds is a lanthanide compound.

80. (Original) The kit of claim 78, wherein said one or more metal compounds are selected from the group consisting of compounds of magnesium, manganese, europium, lanthanum, gadolinium and terbium.

Application No. 09/938,728
Reply to Office Action dated: August 15, 2003

81. (Original) The kit of claim 78, wherein said Protein C activator is a thrombomodulin.

82. (Original) The kit of claim 81, wherein said thrombomodulin is a natural thrombomodulin.

83. (Original) The kit of claim 81, wherein said thrombomodulin is a recombinant thrombomodulin.

84. (Original) The kit of claim 78, further comprising a transfer pipette.

85. (Previously presented) The reagent of Claim 21, wherein said reagent is thrombomodulin or recombinant thrombomodulin.

86. (Previously presented) The reagent of Claim 21, wherein said one or more metals is at least one member selected from the group consisting of cerium, praseodymium, neodymium, promethium, samarium, europium, gadolinium, terbium, dysprosium, holmium, erbium, thulium, ytterbium, and lutetium.

87. (Previously presented) The reagent of Claim 86, wherein said reagent is thrombomodulin or recombinant thrombomodulin.